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WHAT IS CLAIMED IS:

1	1. A method of controlling cancer suppression in a mammal having a
2	cancer suppressing gene, comprising the steps of:
3	making a substantially duplicated genetic material corresponding to the
4	genetic material of said gene, the substantially duplicated material selected from the group
5	consisting of a cloned cancer suppressing gene, a modified or defective cancer suppressing
6	gene, homologues thereof, fragments thereof, and mixtures thereof; and
7	interchanging said duplicated genetic material and the cancer suppressing gene
8	of the mammal.
1	2. A method of claim 1, wherein before said making a substantially
2	duplicated genetic material, determining the chromosomal location of said cancer suppressing
3	gene of the mammal.
1	3. A method of claim 1, wherein after said making a substantially
2	duplicated genetic material, detecting the presence or absence of an inactive cancer
3	suppressing gene of a tissue sample of the mammal to determine whether or not the tissue
4	sample cancer suppressing gene is defective or absent.
1	4. A method of claim 3, wherein in response to a determination that the
2	tissue sample cancer suppressing gene is either defective or absent, replacing a cancer
3	suppressing gene of the mammal with its clone.
1	5. A method of claim 3, wherein the determination of whether or not the
2	tissue sample cancer suppressing gene is defective or absent is accomplished by measuring
3	the amount of protein product of said cancer suppressing gene, of the tissue sample, bound by
4	an antibody specific for said protein.
•	6 A mathed of claims 5 whomein the determination of whether or not the
1	6. A method of claim 5, wherein the determination of whether or not the
2	tissue sample cancer suppressing gene is defective or absent is accomplished by:
3	(a) labeling said tissue sample with radioactive isotope;
4	(b) lysing the labeled tissue;
5	(c) reacting the protein product of said cancer suppressing gene with an
6 .	antibody specific for said protein thereby forming a protein/antibody immunocomplex;
7	(d) autoradiographing the immunocomplex obtained in step (c); and

8	(e) determining the presence or absence of the protein product by
9	comparing the autoradiogram of step (d) with the autoradiogram of the standard protein
0	product.
1	7. The method of claim 5, wherein the determination of whether or not
2	the tissue sample cancer suppressing gene is defective or absent is accomplished by enzyme
3	immunoassay techniques.
ڔ	immunoassay toomiques.
1	8. The method of claim 5, wherein the determination of whether or not
2	the tissue sample cancer suppressing gene is defective or absent is accomplished by
3	immunócytochemistry methods.
1	9. The method of claim 5, wherein the cancer suppressing gene is the RB
2	gene and the protein product is ppRB ¹¹⁰ .
_	gone and the protein product is ppres
1	10. The method of claim 1, wherein said cancer suppressing gene is
2	replaced with substantially duplicated material selected from the group consisting of said
3	cloned cancer suppressing gene, homologues thereof, fragments thereof, and mixtures
4	thereof, for therapeutic purposes.
1	11. The method of claim 1, wherein said cancer suppressing gene is
2	replaced with substantially duplicated material selected from the group consisting of said
3	defective cancer suppressing gene, homologues thereof, fragments thereof, and mixtures
	thereof, for facilitating the testing of the carcinogenicity of environmental influences.
4	mereor, for facilitating the testing of the caremogenicity of charleman influences.
1	12. The method of claim 2, wherein the location of said cancer suppressing
2	gene is determined by chromosome walking.
1	13. The method of claim 2, wherein the location of said cancer suppressing
2	gene is determined through organic markers.
4	gene is determined unough organic markers.
1	14. A method of claim 2, wherein:
2	said chromosomal location of said cancer suppressing gene is determined by
3	testing genes of a chromosome for phenotypic expression;
4	determining one of the genes of said chromosome to be a marker gene; and
5	using chromosomal walking techniques to locate a cancer suppressing gene.

1	15. An animal genetically altered so as to have the allele of at least one
2	cancer suppressing gene selected from the group consisting of a defective allele, a homologue
3	thereof, a fragment thereof, and a mixture thereof.
1	16. An animal of claim 15, wherein said defective allele is selected from
2	the group consisting of defective alleles of RB genes, breast cancer suppressing genes,
3	Wilm's tumor suppressing genes, Beckwith-Wiedemann syndrome suppressing genes,
4	bladder transitional cell carcinoma suppressing genes, neuroblastoma suppressing genes,
5	small cell lung carcinoma suppressing genes, renal cell carcinoma suppressing genes,
6	acoustic neuroma suppressing genes, colorectal carcinoma suppressing genes, homolgues
7	thereof, fragments thereof, and mixtures thereof.
1	17. An animal of claim 15, wherein said allele contains a DNA fragment
2	having at least one defective nucleotide sequence.
1	18. An animal of claim 15, wherein said defective allele contains a DNA
2	fragment having at least one defective RB nucleotide sequence.
1	19. The animal of claim 15, wherein said animal is a mouse.
1	20. A method for determining the carcinogenicity of suspected
2	environmental influences, using the animal of claim 14, comprising the steps of:
3	exposing said animal to a suspected environmental influence;
4	observing the animal for the phenotypic expression of cancer; and
5	determining carcinogenicity of the suspected environmental influence in
6	response to observing a phenotypic expression of cancer in the animal.
1	21. A method of claim 20, wherein said exposing includes exposing to a
2	source of radiation.
∠	source of fadiation.
1	22. A method of claim 20, wherein said exposing includes exposing to
2	tobacco combustion products.
1	23. A method of claim 20, wherein said exposing includes exposing to
2	food additives.

1	24. A method of claim 20, wherein said exposing includes exposing to
2	artificial substances.
1	25. A method of claim 20, wherein said observing includes examining the
2	animal for tumor development.
1	26. A method of claim 25, wherein in response to the formation of a tumor
2	in the animal, analyzing the tumor for the presence of cancer cells.
1	27. A method of making the animal of claim 15, comprising:
2	using at least one allele of an animal cancer suppressing gene selected from
	the group consisting of a defective allele, a homologue thereof, a fragment thereof, and a
3	
4	mixture thereof;
5	mutating at least one animal cell with said allele to form a mutated cell;
6	introducing said mutated cell into an animal blastocyst;
7	permitting growth of the blastocyst for a given period of time sufficient to
8	incorporate said allele into its cells; repressing genetic recombinations within said cells;
9	transferring the blastocyst containing said allele into the uterus of a pseudo pregnant animal
10	for giving birth subsequently to an animal bearing said allele;
11	breeding said animal to reproduce additional animals; and
12	selecting the animal of claim 14 from said additional animals by determining
13	the presence therein of the said allele.
1	28. A method of claim 27, wherein before introducing said allele,
2	removing said blastocyst from a super ovulated animal, and wherein said blastocyst is
3	comprised of undifferentiated cells.
1	29. A method of claim 27, wherein said introducing is performed in vitro.
1	30. A pharmaceutical composition wherein the active ingredient is selected
2	from the group consisting of a naturally occurring intact cancer suppressing gene, a cloned
3	intact cancer suppressing gene, fragments thereof, homolgues thereof and mixtures thereof.
1	31. A pharmaceutical composition of claim 30, wherein said naturally
2	occurring and cloned cancer suppressing gene is selected from the group consisting of RB
3	genes, breast cancer suppressing genes, Wilm's tumor suppressing genes, Beckwith-

- 4 Wiedemann syndrome suppressing genes, bladder transitional cell carcinoma suppressing
- 5 genes, neuroblastoma suppressing genes, small cell lung carcinoma suppressing genes, renal
- 6 cell carcinoma suppressing genes, acoustic neuroma suppressing genes, colorectal carcinoma
- 7 suppressing genes, homolgues thereof, fragments thereof, and mixtures thereof.
- 1 32. A pharmaceutical composition of claim 30, wherein the active
- 2 ingredient is selected from the group consisting of RB cDNA, modified RB cDNA fragment,
- 3 clones thereof, homolgues thereof and mixtures thereof.

3

- 1 33. A pharmaceutical composition of claim 31, wherein the active
- 2 ingredient for each of said gene is selected from the group consisting od cDNA of said gene,
- 3 fragments of said cDNA, homologues thereof and mixtures thereof.
- 1 34. A pharmaceutical composition of claim 32, wherein the cancer
- 2 suppressing gene is isolated from human chromosome 13 region 13q14.
- 1 35. A pharmaceutical composition of claim 31, wherein the cancer
- 2 suppressing gene and its clone each has the following nucleotide sequence:

4 5	TTC	CGGT	r TT '	rctc2	AGGG	GA CO	GTTG?	AAAT'	r AT	rttt(GTAA	CGG	GAGT	CGG (GAGA	GACGG		60
6 7 8	GGC	GTGC	ccc (GCGT	3CGC(GC G	CGTC	TCC:	r cc	CCGG	CGCT	CCT	CCAC	AGC '	rcgc	rggctc	:	120
9 10 11 12	CCG	CCGC	GGA 7	AAGG(CGTC										GCC Ala 10	_	:	171
13 14 15 16															CCG Pro		2	219
17 18 19 20															CTG Leu		2	267
21 22 23 24															ACT Thr	GCA Ala	3	315
25 26 27 28															GCT Ala		3	363
29 30 31 32															GGT Gly 90		4	411

33 34 35 36									GCA Ala	459
37 38 39 40		CTA Leu 110								507
41 42 43 44		ATC Ile								555
45 46 47 48		ACC Thr								603
49 50 51 52		TTG. Leu								651
53 54 55 56		TTG Leu								699
57 58 59 60		GTG Val 190							GGG Gly	747
61 62 63		TTA Leu							ATG Met	795
64 65 66 67	TGT	GTC Val		TTT						843
68 69 70 71		CCA Pro								891
72 73 74 75		AGG Arg					Ala			939
76 77 78 79		GAT Asp 270								987
80 81 82 83		GAT Asp								1035
84 85 86 87		TCT Ser								1083
88 89 90 91		TCT Ser								1131
92 93		AGA Arg								1179

94				335					340					345			
95 96	מדמ	GAC	ልርጥ	արար	GDD	ACA	CAG	AGA	ልሮል	CCA	CGA	ΔΔΔ	AGT	AAC	СТТ	GAT	1227
97						Thr			_								J. 22 2.
98		_	350					355					360				
99	<i>α</i>	G 3 G	a=a	3 3 C	C TO N	3 mm	COM	CCA	C 7 C	3 (7 C)	~~ n	amm	אממ	7 CT	CITITI	እ መ ረግ	1275
100 101						ATT Ile											12/5
102	QIU	365	•	11011	vai		370					375	5				
103																	
104	·					TTA											1323
105 106	380	Tnr	тте	Gin	GIN	Leu 385	Met	Met	тте	Leu	390	ser	АТА	ser	Asp	395	
107	200					505											
108						ATT											1371
109	Pro	Ser	Glu	Asn		Ile	Ser	Tyr	Phe		Asn	Сув	Thr	Val		Pro	
110 111					400					405					410		
112	AAA	GAA	AGT	ATA	CTG	AAA	AGA	GTG	AAG	GAT	ATA	GGA	TAC	ATC	TTT	AAA	1419
113	Lys	Glu	Ser	Ile	Leu	Lys	Arg	Val	Lys	Asp	Ile	Gly	Tyr	Ile	Phe	Lys	
114				415					420					425			
115 116	GAG	7 7 7	ттт	ССТ	מממ	GCT	GTG	GGA	CAG	GGT	тст	GTC	GAA	АТТ	GGA	TCA	1467
117						Ala											
118		4	430		•			435		-	-		440		_		
119						~~~		~~~				CC.	G.E.N.	3 mg	~ ~ ~	TOO	2515
120 121						GGA Gly							_		_		1515
122	GIII	445	туг	цуб	пец	Gry	450	A-9	БСС	- y -	- y -	455	val	1100	014		
123																	
												_ ~					
124																C AAA	1563
125	Met					Glu					Ile						1563
																Lys	1563
125 126 127 128	Met 460 CTT	Leu	Lys AAT	Ser GAC	Glu AAC	Glu 465 ATT	Glu TTT	Arg CAT	Leu ATG	Ser TCT	Ile 470 TTA	Gln TTG	Asn GCG	Phe TGC	Ser GCT	Lys 475 CTT	1611
125 126 127 128 129	Met 460 CTT	Leu	Lys AAT	Ser GAC	Glu AAC Asn	Glu 465	Glu TTT	Arg CAT	Leu ATG	Ser TCT Ser	Ile 470 TTA	Gln TTG	Asn GCG	Phe TGC	Ser GCT Ala	Lys 475 CTT	
125 126 127 128 129 130	Met 460 CTT	Leu	Lys AAT	Ser GAC	Glu AAC	Glu 465 ATT	Glu TTT	Arg CAT	Leu ATG	Ser TCT	Ile 470 TTA	Gln TTG	Asn GCG	Phe TGC	Ser GCT	Lys 475 CTT	
125 126 127 128 129 130 131 132	Met 460 CTT Leu GAG	Leu CTG Leu GTT	Lys AAT Asn GTA	Ser GAC Asp	Glu AAC Asn 480 GCC	Glu 465 ATT Ile	Glu TTT Phe	Arg CAT His	Leu ATG Met	TCT Ser 485	Ile 470 TTA Leu ACA	Gln TTG Leu TCT	Asn GCG Ala CAG	Phe TGC Cys	GCT Ala 490 CTT	Lys 475 CTT Leu GAT	
125 126 127 128 129 130 131 132 133	Met 460 CTT Leu GAG	Leu CTG Leu GTT	Lys AAT Asn GTA	Ser GAC Asp ATG Met	AAC Asn 480 GCC	Glu 465 ATT Ile	Glu TTT Phe	Arg CAT His	Leu ATG Met AGA Arg	TCT Ser 485	Ile 470 TTA Leu ACA	Gln TTG Leu TCT	Asn GCG Ala CAG	TGC Cys AAT Asn	GCT Ala 490 CTT	Lys 475 CTT Leu GAT	1611
125 126 127 128 129 130 131 132 133	Met 460 CTT Leu GAG	Leu CTG Leu GTT	Lys AAT Asn GTA	Ser GAC Asp	AAC Asn 480 GCC	Glu 465 ATT Ile	Glu TTT Phe	Arg CAT His	Leu ATG Met	TCT Ser 485	Ile 470 TTA Leu ACA	Gln TTG Leu TCT	Asn GCG Ala CAG	Phe TGC Cys	GCT Ala 490 CTT	Lys 475 CTT Leu GAT	1611
125 126 127 128 129 130 131 132 133	Met 460 CTT Leu GAG Glu	Leu CTG Leu GTT Val	Lys AAT Asn GTA Val	GAC Asp ATG Met 495	AAC Asn 480 GCC Ala	Glu 465 ATT Ile ACA Thr	Glu TTT Phe TAT Tyr	CAT His AGC Ser	ATG Met AGA Arg 500	TCT Ser 485 AGT Ser	Ile 470 TTA Leu ACA Thr	TTG Leu TCT Ser	Asn GCG Ala CAG Gln	TGC Cys AAT Asn 505	GCT Ala 490 CTT Leu	Lys 475 CTT Leu GAT Asp	1611
125 126 127 128 129 130 131 132 133 134 135 136 137	Met 460 CTT Leu GAG Glu	Leu CTG Leu GTT Val	Lys AAT Asn GTA Val	GAC Asp ATG Met 495 GAT	AAC Asn 480 GCC Ala	Glu 465 ATT Ile	Glu TTT Phe TAT Tyr	CAT His AGC Ser	ATG Met AGA Arg 500	TCT Ser 485 AGT Ser	Ile 470 TTA Leu ACA Thr	TTG Leu TCT Ser	Asn GCG Ala CAG Gln GTG Val	TGC Cys AAT Asn 505 CTT	GCT Ala 490 CTT Leu	Lys 475 CTT Leu GAT Asp	1611 1659
125 126 127 128 129 130 131 132 133 134 135 136 137 138	Met 460 CTT Leu GAG Glu	Leu CTG Leu GTT Val	Lys AAT Asn GTA Val	GAC Asp ATG Met 495 GAT	AAC Asn 480 GCC Ala	Glu 465 ATT Ile ACA Thr	Glu TTT Phe TAT Tyr	CAT His AGC Ser	ATG Met AGA Arg 500	TCT Ser 485 AGT Ser	Ile 470 TTA Leu ACA Thr	TTG Leu TCT Ser	Asn GCG Ala CAG Gln GTG	TGC Cys AAT Asn 505 CTT	GCT Ala 490 CTT Leu	Lys 475 CTT Leu GAT Asp	1611 1659
125 126 127 128 129 130 131 132 133 134 135 136 137 138 139	Met 460 CTT Leu GAG Glu TCT Ser	Leu CTG Leu GTT Val GGA Gly	Lys AAT Asn GTA Val ACA Thr 510	GAC Asp ATG Met 495 GAT Asp	AAC Asn 480 GCC Ala TTG Leu	Glu 465 ATT Ile ACA Thr	Glu TTT Phe TAT Tyr	CAT His AGC Ser CCA Pro 515	ATG Met AGA Arg 500 TGG Trp	TCT Ser 485 AGT Ser ATT	Ile 470 TTA Leu ACA Thr	TTG Leu TCT Ser AAT Asn	Asn GCG Ala CAG Gln GTG Val 520	TGC Cys AAT Asn 505 CTT Leu	GCT Ala 490 CTT Leu AAT Asn	Lys 475 CTT Leu GAT Asp TTA Leu	1611 1659 1707
125 126 127 128 129 130 131 132 133 134 135 136 137 138	Met 460 CTT Leu GAG Glu TCT Ser	CTG Leu GTT Val GGA Gly	AAT Asn GTA Val ACA Thr 510	GAC Asp ATG Met 495 GAT Asp	AAC Asn 480 GCC Ala TTG Leu	Glu 465 ATT Ile ACA Thr TCT Ser	Glu TTT Phe TAT Tyr TTC Phe	CAT His AGC Ser CCA Pro 515 GTG	Leu ATG Met AGA Arg 500 TGG Trp	TCT Ser 485 AGT Ser ATT Ile	Ile 470 TTA Leu ACA Thr CTG Leu	TTG Leu TCT Ser AAT Asn	Asn GCG Ala CAG Gln GTG Val 520 ATC	TGC Cys AAT Asn 505 CTT Leu	GCT Ala 490 CTT Leu AAT Asn	Lys 475 CTT Leu GAT Asp TTA Leu	1611 1659
125 126 127 128 129 130 131 132 133 134 135 136 137 138 139 140 141 142	Met 460 CTT Leu GAG Glu TCT Ser	CTG Leu GTT Val GGA Gly	AAT Asn GTA Val ACA Thr 510	GAC Asp ATG Met 495 GAT Asp	AAC Asn 480 GCC Ala TTG Leu	Glu 465 ATT Ile ACA Thr	Glu TTT Phe TAT Tyr TTC Phe	CAT His AGC Ser CCA Pro 515 GTG	Leu ATG Met AGA Arg 500 TGG Trp	TCT Ser 485 AGT Ser ATT Ile	Ile 470 TTA Leu ACA Thr CTG Leu	TTG Leu TCT Ser AAT Asn	Asn GCG Ala CAG Gln GTG Val 520 ATC	TGC Cys AAT Asn 505 CTT Leu	GCT Ala 490 CTT Leu AAT Asn	Lys 475 CTT Leu GAT Asp TTA Leu	1611 1659 1707
125 126 127 128 129 130 131 132 133 134 135 136 137 138 139 140 141 142 143	Met 460 CTT Leu GAG Glu TCT Ser	CTG Leu GTT Val GGA Gly GCC Ala 525	AAT Asn GTA Val ACA Thr 510 TTT Phe	GAC Asp ATG Met 495 GAT Asp	AAC Asn 480 GCC Ala TTG Leu	Glu 465 ATT Ile ACA Thr TCT Ser	Glu TTT Phe TAT Tyr TTC Phe AAA Lys 530	CAT His AGC Ser CCA Pro 515 GTG Val	Leu ATG Met AGA Arg 500 TGG Trp	TCT Ser 485 AGT Ser ATT Ile	Ile 470 TTA Leu ACA Thr CTG Leu AGT Ser	TTG Leu TCT Ser AAT Asn TTT Phe 535	Asn GCG Ala CAG Gln GTG Val 520 ATC Ile	TGC Cys AAT Asn 505 CTT Leu AAA Lys	GCT Ala 490 CTT Leu AAT Asn GCA Ala	Lys 475 CTT Leu GAT Asp TTA Leu GAA Glu	1611 1659 1707
125 126 127 128 129 130 131 132 133 134 135 136 137 138 139 140 141 142 143 144	Met 460 CTT Leu GAG Glu TCT Ser AAA Lys	Leu CTG Leu GTT Val GGA Gly GCC Ala 525 AAC	Lys AAT Asn GTA Val ACA Thr 510 TTT Phe	GAC Asp ATG Met 495 GAT Asp GAT Asp	AAC Asn 480 GCC Ala TTG Leu TTT Phe	Glu 465 ATT Ile ACA Thr TCT Ser TAC Tyr	Glu TTT Phe TAT Tyr TTC Phe AAA Lys 530 ATG	Arg CAT His AGC Ser CCA Pro 515 GTG Val	Leu ATG Met AGA Arg 500 TGG Trp ATC Ile	TCT Ser 485 AGT Ser ATT Ile GAA Glu	Ile 470 TTA Leu ACA Thr CTG Leu AGT Ser	TTG Leu TCT Ser AAT Asn TTT Phe 535 GAA	Asn GCG Ala CAG Gln GTG Val 520 ATC Ile CGA	Phe TGC Cys AAT Asn 505 CTT Leu AAA Lys	GCT Ala 490 CTT Leu AAT Asn GCA Ala	Lys 475 CTT Leu GAT Asp TTA Leu GAA Glu CAT	1611 1659 1707
125 126 127 128 129 130 131 132 133 134 135 136 137 138 139 140 141 142 143	Met 460 CTT Leu GAG Glu TCT Ser AAA Lys	Leu CTG Leu GTT Val GGA Gly GCC Ala 525 AAC	Lys AAT Asn GTA Val ACA Thr 510 TTT Phe	GAC Asp ATG Met 495 GAT Asp GAT Asp	AAC Asn 480 GCC Ala TTG Leu TTT Phe	Glu 465 ATT Ile ACA Thr TCT Ser	Glu TTT Phe TAT Tyr TTC Phe AAA Lys 530 ATG	Arg CAT His AGC Ser CCA Pro 515 GTG Val	Leu ATG Met AGA Arg 500 TGG Trp ATC Ile	TCT Ser 485 AGT Ser ATT Ile GAA Glu	Ile 470 TTA Leu ACA Thr CTG Leu AGT Ser	TTG Leu TCT Ser AAT Asn TTT Phe 535 GAA	Asn GCG Ala CAG Gln GTG Val 520 ATC Ile CGA	Phe TGC Cys AAT Asn 505 CTT Leu AAA Lys	GCT Ala 490 CTT Leu AAT Asn GCA Ala	Lys 475 CTT Leu GAT Asp TTA Leu GAA Glu CAT	1611 1659 1707
125 126 127 128 129 130 131 132 133 134 135 136 137 138 139 140 141 142 143 144 145 146 147	Met 460 CTT Leu GAG Glu TCT Ser AAA Lys GGC Gly 540	Leu CTG Leu GTT Val GGA Gly GCC Ala 525 AAC Asn	Lys AAT Asn GTA Val ACA Thr 510 TTT Phe TTG Leu	GAC Asp ATG Met 495 GAT Asp GAT Asp	AAC Asn 480 GCC Ala TTG Leu TTT Phe	Glu 465 ATT Ile ACA Thr TCT Ser TAC Tyr GAA Glu 545	Glu TTT Phe TAT Tyr TTC Phe AAA Lys 530 ATG Met	CAT His AGC Ser CCA Pro 515 GTG Val	Leu ATG Met AGA Arg 500 TGG Trp ATC Ile AAA Lys	TCT Ser 485 AGT Ser ATT Ile GAA Glu CAT His	Ile 470 TTA Leu ACA Thr CTG Leu AGT Ser TTA Leu 550	TTG Leu TCT Ser AAT Asn TTT Phe 535 GAA Glu	Asn GCG Ala CAG Gln GTG Val 520 ATC Ile CGA Arg	TGC Cys AAT Asn 505 CTT Leu AAA Lys	GCT Ala 490 CTT Leu AAT ASN GCA Ala GAA Glu	Lys 475 CTT Leu GAT Asp TTA Leu GAA Glu CAT His 555	1611 1659 1707 1755
125 126 127 128 129 130 131 132 133 134 135 136 137 138 139 140 141 142 143 144 145 146 147 148	Met 460 CTT Leu GAG Glu TCT Ser AAA Lys GGC Gly 540 CGA	Leu CTG Leu GTT Val GGA Gly GCC Ala 525 AAC Asn	Lys AAT Asn GTA Val ACA Thr 510 TTT Phe TTG Leu ATG	GAC Asp ATG Met 495 GAT Asp GAT Asp ACA Thr	AAC Asn 480 GCC Ala TTG Leu TTT Phe AGA Arg	Glu 465 ATT Ile ACA Thr TCT Ser TAC Tyr GAA Glu 545 CTT	Glu TTT Phe TAT Tyr TTC Phe AAA Lys 530 ATG Met	Arg CAT His AGC Ser CCA Pro 515 GTG Val ATA Ile	Leu ATG Met AGA Arg 500 TGG Trp ATC Ile AAA Lys	TCT Ser 485 AGT Ser ATT Ile GAA Glu CAT His	Ile 470 TTA Leu ACA Thr CTG Leu AGT Ser TTA Leu 550 GAT	Gln TTG Leu TCT Ser AAT Asn TTT Phe 535 GAA Glu TCA	Asn GCG Ala CAG Gln GTG Val 520 ATC Ile CGA Arg	TGC Cys AAT Asn 505 CTT Leu AAA Lys TGT Cys	GCT Ala 490 CTT Leu AAT Asn GCA Ala GAA Glu TTT	Lys 475 CTT Leu GAT Asp TTA Leu GAA Glu CAT His 555 GAT	1611 1659 1707
125 126 127 128 129 130 131 132 133 134 135 136 137 138 139 140 141 142 143 144 145 146 147 148 149	Met 460 CTT Leu GAG Glu TCT Ser AAA Lys GGC Gly 540 CGA	Leu CTG Leu GTT Val GGA Gly GCC Ala 525 AAC Asn	Lys AAT Asn GTA Val ACA Thr 510 TTT Phe TTG Leu ATG	GAC Asp ATG Met 495 GAT Asp GAT Asp ACA Thr	Glu AAC Asn 480 GCC Ala TTG Leu TTT Phe AGA Arg	Glu 465 ATT Ile ACA Thr TCT Ser TAC Tyr GAA Glu 545	Glu TTT Phe TAT Tyr TTC Phe AAA Lys 530 ATG Met	Arg CAT His AGC Ser CCA Pro 515 GTG Val ATA Ile	Leu ATG Met AGA Arg 500 TGG Trp ATC Ile AAA Lys	TCT Ser 485 AGT Ser ATT Ile GAA Glu CAT His	Ile 470 TTA Leu ACA Thr CTG Leu AGT Ser TTA Leu 550 GAT	Gln TTG Leu TCT Ser AAT Asn TTT Phe 535 GAA Glu TCA	Asn GCG Ala CAG Gln GTG Val 520 ATC Ile CGA Arg	TGC Cys AAT Asn 505 CTT Leu AAA Lys TGT Cys	GCT Ala 490 CTT Leu AAT ASN GCA Ala GAA Glu TTT Phe	Lys 475 CTT Leu GAT Asp TTA Leu GAA Glu CAT His 555 GAT	1611 1659 1707 1755
125 126 127 128 129 130 131 132 133 134 135 136 137 138 139 140 141 142 143 144 145 146 147 148	Met 460 CTT Leu GAG Glu TCT Ser AAA Lys GGC Gly 540 CGA	Leu CTG Leu GTT Val GGA Gly GCC Ala 525 AAC Asn	Lys AAT Asn GTA Val ACA Thr 510 TTT Phe TTG Leu ATG	GAC Asp ATG Met 495 GAT Asp GAT Asp ACA Thr	AAC Asn 480 GCC Ala TTG Leu TTT Phe AGA Arg	Glu 465 ATT Ile ACA Thr TCT Ser TAC Tyr GAA Glu 545 CTT	Glu TTT Phe TAT Tyr TTC Phe AAA Lys 530 ATG Met	Arg CAT His AGC Ser CCA Pro 515 GTG Val ATA Ile	Leu ATG Met AGA Arg 500 TGG Trp ATC Ile AAA Lys	TCT Ser 485 AGT Ser ATT Ile GAA Glu CAT His	Ile 470 TTA Leu ACA Thr CTG Leu AGT Ser TTA Leu 550 GAT	Gln TTG Leu TCT Ser AAT Asn TTT Phe 535 GAA Glu TCA	Asn GCG Ala CAG Gln GTG Val 520 ATC Ile CGA Arg	TGC Cys AAT Asn 505 CTT Leu AAA Lys TGT Cys	GCT Ala 490 CTT Leu AAT Asn GCA Ala GAA Glu TTT	Lys 475 CTT Leu GAT Asp TTA Leu GAA Glu CAT His 555 GAT	1611 1659 1707 1755
125 126 127 128 129 130 131 132 133 134 135 136 137 138 139 140 141 142 143 144 145 146 147 148 149 150 151 152	Met 460 CTT Leu GAG Glu TCT Ser AAA Lys GGC Gly 540 CGA Arg	Leu CTG Leu GTT Val GGA Gly GCC Ala 525 AAC Asn ATC Ile ATT	Lys AAT Asn GTA Val ACA Thr 510 TTT Phe TTG Leu ATG Met	GAC Asp ATG Met 495 GAT Asp GAT Asp ACA Thr GAA Glu CAA	Glu AAC Asn 480 GCC Ala TTG Leu TTT Phe AGA Arg TCC Ser 560 TCA	Glu 465 ATT Ile ACA Thr TCT Ser TAC Tyr GAA Glu 545 CTT Leu AAG	Glu TTT Phe TAT Tyr TTC Phe AAA Lys 530 ATG Met GCA Ala GAC	CAT His AGC Ser CCA Pro 515 GTG Val ATA Ile TGG Trp	Leu ATG Met AGA Arg 500 TGG Trp ATC Ile AAA Lys CTC Leu GAA	TCT Ser 485 AGT Ser ATT Ile GAA Glu CAT His TCA Ser 565 GGA	Ile 470 TTA Leu ACA Thr CTG Leu AGT Ser TTA Leu 550 GAT Asp	TTG Leu TCT Ser AAT Asn TTT Phe 535 GAA Glu TCA Ser ACT	Asn GCG Ala CAG Gln GTG Val 520 ATC Ile CGA Arg CCT Pro	TGC Cys AAT Asn 505 CTT Leu AAA Lys TGT Cys TTA Leu	GCT Ala 490 CTT Leu AAT Asn GCA Ala Glu TTT Phe 570 CTT	Lys 475 CTT Leu GAT Asp TTA Leu GAA Glu CAT His 555 GAT Asp	1611 1659 1707 1755
125 126 127 128 129 130 131 132 133 134 135 136 137 138 139 140 141 142 143 144 145 146 147 148 149 150 151	Met 460 CTT Leu GAG Glu TCT Ser AAA Lys GGC Gly 540 CGA Arg	Leu CTG Leu GTT Val GGA Gly GCC Ala 525 AAC Asn ATC Ile ATT	Lys AAT Asn GTA Val ACA Thr 510 TTT Phe TTG Leu ATG Met	GAC Asp ATG Met 495 GAT Asp GAT Asp ACA Thr GAA Glu CAA	Glu AAC Asn 480 GCC Ala TTG Leu TTT Phe AGA Arg TCC Ser 560 TCA	Glu 465 ATT Ile ACA Thr TCT Ser TAC Tyr GAA Glu 545 CTT Leu	Glu TTT Phe TAT Tyr TTC Phe AAA Lys 530 ATG Met GCA Ala GAC	CAT His AGC Ser CCA Pro 515 GTG Val ATA Ile TGG Trp	Leu ATG Met AGA Arg 500 TGG Trp ATC Ile AAA Lys CTC Leu GAA	TCT Ser 485 AGT Ser ATT Ile GAA Glu CAT His TCA Ser 565 GGA	Ile 470 TTA Leu ACA Thr CTG Leu AGT Ser TTA Leu 550 GAT Asp	TTG Leu TCT Ser AAT Asn TTT Phe 535 GAA Glu TCA Ser ACT	Asn GCG Ala CAG Gln GTG Val 520 ATC Ile CGA Arg CCT Pro	TGC Cys AAT Asn 505 CTT Leu AAA Lys TGT Cys TTA Leu	GCT Ala 490 CTT Leu AAT Asn GCA Ala Glu TTT Phe 570 CTT	Lys 475 CTT Leu GAT Asp TTA Leu GAA Glu CAT His 555 GAT Asp	1611 1659 1707 1755 1803

															GCA	19
Ser	Ala	Cys 590	Pro	Leu	Asn	Leu	Pro 595	Leu	Gln	Asn	Asn	His 600	Thr	Ala	Ala	
GAT	ATG	TAT	CTT	тст	CCT	GTA	AGA	тст	CCA	AAG	AAA	AAA	GGT	TCA	ACT	19
Asp	Met 605	Tyr	Leu	Ser	Pro	Val 610	Arg	Ser	Pro	ГÀг	Lys 615	Lys	Gly	Ser	Thr	
														TCA Ser	_	20
620	Arg	vai	A511	501	625	AIG	Abii	ALG		630	0111	ALG	±114-	001	635	
ጥጥር	CAG	ACC	CAG	AAG	CCA	ጥጥር፤	ΔΔΔ	ጥርጥ	ACC	ጥረጥ	СТТ	тса	СТС	$\mathbf{T}\mathbf{T}\mathbf{T}$	ТАТ	20
														Phe		2,0
				640					645					650		
AAA	AAA	GTG	TAT	CGG	CTA	GCC	TAT	CTC	CGG	СТА	AAT	ACA	CTT	TGT	GAA	21
Lys	Lys	Val	_	Arg	Leu	Ala	Tyr	Leu 660	Arg	Leu	Asn	Thr	Leu 665	Cys	Glu	
			655					880					005			
														ACC		21
Arg	ьeu	Leu 670	ser	GIU	HIS	Pro	675	ьeu	GIU	HIS	TTE	680	тър	Thr	Бец	
	~~~	~~~		ana.	a. a		~~~		<b>~~~</b>	ama	7 m/3	202	a a a	7.00	Cam	2.5
														AGG Arg		22
	685					690		-			695		_			
TT	G GA	CA	TA	r ATO	3 ATC	G TGT	r TC	CATO	TAT	r ggd	CATA	TG(	CAA	A GTO	AAG	2
Leu					Met					Gly				A GTO Val	Lys	2
																2
Leu 700 AAT	Asp	Gln GAC	Ile	Met AAA	Met 705 TTC	Cys AAA	Ser ATC	Met ATT	Tyr GTA	Gly 710 ACA	Ile GCA	Cys	Lys	Val GAT	Lys 715 CTT	
Leu 700 AAT	Asp	Gln GAC	Ile	Met AAA Lys	Met 705 TTC	Cys AAA	Ser ATC	Met ATT	Tyr GTA	Gly 710 ACA	Ile GCA	Cys	Lys	Val	Lys 715 CTT	
Leu 700 AAT Asn	Asp ATA Ile	Gln GAC Asp	Ile CTT Leu	Met AAA Lys 720	Met 705 TTC Phe	Cys AAA Lys	Ser ATC Ile	Met ATT Ile	Tyr GTA Val 725	Gly 710 ACA Thr	Ile GCA Ala	Cys TAC Tyr	Lys AAG Lys	Val GAT Asp 730	Lys 715 CTT Leu	23
Leu 700 AAT Asn	ASP ATA Ile CAT	Gln GAC Asp	Ile CTT Leu GTT	Met  AAA Lys 720 CAG	Met 705 TTC Phe	Cys AAA Lys ACA	Ser ATC Ile	Met ATT Ile	Tyr GTA Val 725 CGT	Gly 710 ACA Thr	Ile GCA Ala TTG	Cys TAC Tyr ATC	Lys AAG Lys AAA	GAT Asp 730	Lys 715 CTT Leu GAG	23
Leu 700 AAT Asn	ASP ATA Ile CAT	Gln GAC Asp	Ile CTT Leu GTT	Met  AAA Lys 720 CAG	Met 705 TTC Phe	Cys AAA Lys ACA	Ser ATC Ile	Met ATT Ile	Tyr GTA Val 725 CGT	Gly 710 ACA Thr	Ile GCA Ala TTG	Cys TAC Tyr ATC	Lys AAG Lys AAA	Val GAT Asp 730	Lys 715 CTT Leu GAG	23
Leu 700 AAT Asn CCT Pro	ASP ATA Ile CAT His	Gln GAC Asp GCT Ala	CTT Leu GTT Val 735	AAA Lys 720 CAG Gln	Met 705 TTC Phe GAG Glu	Cys AAA Lys ACA Thr	Ser ATC Ile TTC Phe	ATT Ile AAA Lys 740	Tyr GTA Val 725 CGT Arg	Gly 710 ACA Thr GTT Val	Ile GCA Ala TTG Leu	TAC Tyr ATC Ile	Lys AAG Lys AAA Lys 745	GAT Asp 730 GAA Glu	Lys 715 CTT Leu GAG Glu	23
Leu 700 AAT Asn CCT Pro	ASP ATA Ile CAT His	Gln GAC Asp GCT Ala GAT Asp	CTT Leu GTT Val 735	Met  AAA Lys 720  CAG Gln  ATT	Met 705 TTC Phe GAG Glu	Cys  AAA Lys  ACA Thr	Ser ATC Ile TTC Phe	ATT Ile AAA Lys 740	Tyr GTA Val 725 CGT Arg	Gly 710 ACA Thr GTT Val	GCA Ala TTG Leu	TAC Tyr ATC Ile TTC Phe	AAG Lys AAA Lys 745 ATG	GAT Asp 730	Lys 715 CTT Leu GAG Glu	23
Leu 700 AAT Asn CCT Pro	ASP ATA Ile CAT His	Gln GAC Asp GCT Ala	CTT Leu GTT Val 735	Met  AAA Lys 720  CAG Gln  ATT	Met 705 TTC Phe GAG Glu	Cys  AAA Lys  ACA Thr	Ser ATC Ile TTC Phe	ATT Ile AAA Lys 740	Tyr GTA Val 725 CGT Arg	Gly 710 ACA Thr GTT Val	GCA Ala TTG Leu	TAC Tyr ATC Ile	AAG Lys AAA Lys 745 ATG	GAT Asp 730 GAA Glu	Lys 715 CTT Leu GAG Glu	23
Leu 700 AAT Asn CCT Pro GAG Glu	ASP ATA Ile CAT His TAT Tyr	GAC Asp GCT Ala GAT Asp 750 ACA	CTT Leu GTT Val 735 TCT Ser	Met  AAA Lys 720 CAG Gln ATT Ile	Met 705 TTC Phe GAG Glu ATA Ile	Cys  AAA Lys  ACA Thr  GTA Val	Ser ATC Ile TTC Phe TTC Phe 755	Met ATT Ile AAA Lys 740 TAT Tyr	Tyr GTA Val 725 CGT Arg AAC Asn	Gly 710 ACA Thr GTT Val TCG Ser	GCA Ala TTG Leu GTC Val	TAC Tyr ATC Ile TTC Phe 760	Lys  AAG Lys  AAA Lys 745  ATG Met	GAT Asp 730 GAA Glu CAG Gln	Lys 715 CTT Leu GAG Glu AGA Arg	23
Leu 700 AAT Asn CCT Pro GAG Glu	ASP  ATA Ile  CAT His  TAT Tyr  AAA Lys	GAC Asp GCT Ala GAT Asp 750 ACA	CTT Leu GTT Val 735 TCT Ser	Met  AAA Lys 720 CAG Gln ATT Ile	Met 705 TTC Phe GAG Glu ATA Ile	Cys  AAA Lys  ACA Thr  GTA Val  CAG Gln	Ser ATC Ile TTC Phe TTC Phe 755	Met ATT Ile AAA Lys 740 TAT Tyr	Tyr GTA Val 725 CGT Arg AAC Asn	Gly 710 ACA Thr GTT Val TCG Ser	GCA Ala TTG Leu GTC Val	TAC Tyr ATC Ile TTC Phe 760	Lys  AAG Lys  AAA Lys 745  ATG Met	GAT Asp 730 GAA Glu CAG Gln	Lys 715 CTT Leu GAG Glu AGA Arg	23
Leu 700 AAT Asn CCT Pro GAG Glu CTG Leu	ASP  ATA Ile  CAT His  TAT Tyr  AAA Lys 765	GAC Asp GCT Ala GAT Asp 750 ACA Thr	CTT Leu GTT Val 735 TCT Ser AAT Asn	Met  AAA Lys 720 CAG Gln ATT Ile ATT Ile	Met 705 TTC Phe GAG Glu ATA Ile TTG Leu	Cys  AAA Lys  ACA Thr  GTA Val  CAG Gln 770	Ser ATC Ile TTC Phe TTC Tyr	Met ATT Ile AAA Lys 740 TAT Tyr GCT Ala	Tyr GTA Val 725 CGT Arg AAC Asn TCC Ser	Gly 710 ACA Thr GTT Val TCG Ser ACC Thr	GCA Ala TTG Leu GTC Val AGG Arg 775	TAC Tyr ATC Ile TTC Phe 760 CCC Pro	Lys  AAG Lys  AAA Lys  745  ATG Met  CCT Pro	GAT Asp 730 GAA Glu CAG Gln ACC Thr	Lys 715 CTT Leu GAG Glu AGA Arg TTG Leu	23 23 24
Leu 700 AAT Asn CCT Pro GAG Glu CTG Leu	ASP ATA Ile CAT His TAT Tyr AAA Lys 765 CCA	GAC Asp GCT Ala GAT Asp 750 ACA Thr	CTT Leu GTT Val 735 TCT Ser AAT Asn	Met  AAA Lys 720 CAG Gln ATT Ile ATT Ile CAC	Met 705 TTC Phe GAG Glu ATA Ile TTG Leu	Cys  AAA Lys  ACA Thr  GTA Val  CAG Gln 770  CCT	Ser ATC Ile TTC Phe TTC Tyr CGA	Met ATT Ile AAA Lys 740 TAT Tyr GCT Ala AGC	Tyr GTA Val 725 CGT Arg AAC Asn TCC Ser	Gly 710 ACA Thr GTT Val TCG Ser ACC Thr	GCA Ala  TTG Leu  GTC Val  AGG Arg 775 AAG	TAC Tyr ATC Ile TTC Phe 760 CCC Pro	Lys AAG Lys 745 ATG Met CCT Pro	GAT Asp 730 GAA Glu CAG Gln ACC Thr	Lys 715 CTT Leu GAG Glu AGA Arg TTG Leu	23 24 24
Leu 700 AAT Asn CCT Pro GAG Glu CTG Leu	ASP ATA Ile CAT His TAT Tyr AAA Lys 765 CCA	GAC Asp GCT Ala GAT Asp 750 ACA Thr	CTT Leu GTT Val 735 TCT Ser AAT Asn	Met  AAA Lys 720 CAG Gln ATT Ile ATT Ile CAC	Met 705 TTC Phe GAG Glu ATA Ile TTG Leu	Cys  AAA Lys  ACA Thr  GTA Val  CAG Gln 770  CCT	Ser ATC Ile TTC Phe TTC Tyr CGA	Met ATT Ile AAA Lys 740 TAT Tyr GCT Ala AGC	Tyr GTA Val 725 CGT Arg AAC Asn TCC Ser	Gly 710 ACA Thr GTT Val TCG Ser ACC Thr	GCA Ala  TTG Leu  GTC Val  AGG Arg 775 AAG	TAC Tyr ATC Ile TTC Phe 760 CCC Pro	Lys AAG Lys 745 ATG Met CCT Pro	GAT Asp 730 GAA Glu CAG Gln ACC Thr	Lys 715 CTT Leu GAG Glu AGA Arg TTG Leu	23 24 24
Leu 700 AAT Asn CCT Pro GAG Glu CTG Leu TCA Ser 780	ASP  ATA Ile  CAT His  TAT Tyr  AAA Lys 765  CCA Pro	GAC Asp GCT Ala GAT Asp 750 ACA Thr	CTT Leu GTT Val 735 TCT Ser AAT Asn	Met  AAA Lys 720 CAG Gln  ATT Ile  ATT Ile  CAC His	Met 705 TTC Phe GAG Glu ATA Ile TTG Leu ATT Ile 785	Cys AAA Lys ACA Thr GTA Val CAG Gln 770 CCT Pro	Ser ATC Ile TTC Phe 755 TAT Tyr CGA Arg	Met ATT Ile AAA Lys 740 TAT Tyr GCT Ala AGC Ser	Tyr GTA Val 725 CGT Arg AAC Asn TCC Ser CCT Pro	Gly 710 ACA Thr GTT Val TCG Ser ACC Thr TAC Tyr 790	GCA Ala TTG Leu GTC Val AGG Arg 775 AAG Lys	TAC Tyr ATC Ile TTC Phe 760 CCC Pro	Lys AAG Lys AAA Lys 745 ATG Met CCT Pro	GAT Asp 730 GAA Glu CAG Gln ACC Thr	Lys 715 CTT Leu  GAG Glu  AGA Arg  TTG Leu  TCA Ser 795	23 24 24
Leu 700 AAT Asn CCT Pro GAG Glu CTG Leu TCA Ser 780 CCC	ASP  ATA Ile  CAT His  TAT Tyr  AAA Lys 765 CCA Pro	Gln GAC Asp GCT Ala GAT Asp 750 ACA Thr ATA Ile CGG	CTT Leu GTT Val 735 TCT Ser AAT Asn CCT Pro	Met  AAA Lys 720 CAG Gln ATT Ile  ATT Ile  CAC His	Met 705 TTC Phe GAG Glu ATA Ile TTG Leu ATT Ile 785 GGA	Cys  AAA Lys  ACA Thr  GTA Val  CAG Gln 770  CCT Pro	Ser ATC Ile TTC Phe TTC Phe 755 TAT Tyr CGA Arg	Met ATT Ile AAA Lys 740 TAT Tyr GCT Ala AGC Ser	Tyr GTA Val 725 CGT Arg AAC Asn TCC Ser CCT Pro	Gly 710 ACA Thr GTT Val TCG Ser ACC Thr TAC Tyr 790 ATT	GCA Ala  TTG Leu  GTC Val  AGG Arg 775  AAG Lys	TAC Tyr  ATC Ile  TTC Phe 760  CCC Pro  TTT Phe	Lys AAG Lys AAA Lys 745 ATG Met CCT Pro CCT	GAT Asp 730 GAA Glu CAG Gln ACC Thr	Lys 715 CTT Leu  GAG Glu  AGA Arg  TTG Leu  TCA Ser 795 AGT	23 24 24
Leu 700 AAT Asn CCT Pro GAG Glu CTG Leu TCA Ser 780 CCC	ASP  ATA Ile  CAT His  TAT Tyr  AAA Lys 765 CCA Pro	Gln GAC Asp GCT Ala GAT Asp 750 ACA Thr ATA Ile CGG	CTT Leu GTT Val 735 TCT Ser AAT Asn CCT Pro	Met  AAA Lys 720 CAG Gln ATT Ile  ATT Ile  CAC His	Met 705 TTC Phe GAG Glu ATA Ile TTG Leu ATT Ile 785 GGA	Cys  AAA Lys  ACA Thr  GTA Val  CAG Gln 770  CCT Pro	Ser ATC Ile TTC Phe TTC Phe 755 TAT Tyr CGA Arg	Met ATT Ile AAA Lys 740 TAT Tyr GCT Ala AGC Ser	Tyr GTA Val 725 CGT Arg AAC Asn TCC Ser CCT Pro	Gly 710 ACA Thr GTT Val TCG Ser ACC Thr TAC Tyr 790 ATT	GCA Ala  TTG Leu  GTC Val  AGG Arg 775  AAG Lys	TAC Tyr  ATC Ile  TTC Phe 760  CCC Pro  TTT Phe	Lys AAG Lys AAA Lys 745 ATG Met CCT Pro CCT	GAT Asp 730 GAA Glu CAG Gln ACC Thr AGT Ser	Lys 715 CTT Leu  GAG Glu  AGA Arg  TTG Leu  TCA Ser 795 AGT	23 24 24
Leu 700 AAT Asn CCT Pro GAG Glu CTG Leu TCA Ser 780 CCC Pro	ASP  ATA Ile  CAT His  TAT Tyr  AAA Lys 765  CCA Pro  TTA Leu	Gln GAC Asp GCT Ala GAT Asp 750 ACA Thr ATA Ile CGG Arg	Ile CTT Leu GTT Val 735 TCT Ser AAT ASN CCT Pro	Met  AAA Lys 720 CAG Gln ATT Ile  ATT Pro 800	Met 705 TTC Phe GAG Glu ATA Ile TTG Leu ATT Ile 785 GGA Gly	Cys AAA Lys ACA Thr GTA Val  CAG Gln 770 CCT Pro GGG Gly	Ser ATC Ile TTC Phe 755 TAT Tyr CGA Arg AAC Asn	Met ATT Ile AAA Lys 740 TAT Tyr GCT Ala AGC Ser ATC Ile	Tyr GTA Val 725 CGT Arg AAC Asn TCC Ser CCT Pro TAT Tyr 805	Gly 710 ACA Thr GTT Val TCG Ser ACC Thr TAC Tyr 790 ATT Ile	GCA Ala  TTG Leu  GTC Val  AGG Arg 775  AAG Lys  TCA Ser	TAC TYT ATC Ile TTC Phe 760 CCC Pro TTT Phe CCC Pro	Lys AAG Lys AAA Lys 745 ATG Met CCT Pro CTG Leu	GAT Asp 730 GAA Glu CAG Gln ACC Thr AGT Ser	Lys 715 CTT Leu  GAG Glu  AGA Arg  TTG Leu  TCA Ser 795 AGT Ser	23 24 24 25
Leu 700 AAT Asn CCT Pro GAG Glu CTG Leu TCA Ser 780 CCC Pro	ASP  ATA Ile  CAT His  TAT Tyr  AAA Lys 765 CCA Pro  TTA Leu  TAT	GAC Asp GCT Ala GAT Asp 750 ACA Thr ATA Ile CGG Arg	CTT Leu GTT Val 735 TCT Ser AAT Asn CCT Pro ATT Ile	Met  AAA Lys 720 CAG Gln ATT Ile  ATT Ile  CAC His  CCT Pro 800 TCA	Met 705 TTC Phe GAG Glu ATA Ile TTG Leu ATT Ile 785 GGA Gly	Cys  AAA Lys  ACA Thr  GTA Val  CAG Gln 770  CCT Pro  GGG Gly  GGT	Ser ATC Ile TTC Phe TTC Phe 755 TAT Tyr CGA Arg AAC Asn CTG	Met ATT Ile AAA Lys 740 TAT Tyr GCT Ala AGC Ser ATC Ile CCA	Tyr GTA Val 725 CGT Arg AAC Asn TCC Ser CCT Pro TAT Tyr 805 ACA	Gly 710 ACA Thr GTT Val TCG Ser ACC Thr TAC Tyr 790 ATT Ile CCA	GCA Ala  TTG Leu  GTC Val  AGG Arg 775  AAG Lys  TCA Ser  ACA	TAC Tyr  ATC Ile  TTC Phe 760  CCC Pro  TTT Phe  CCC Pro	AAG Lys AAA Lys 745 ATG Met CCT Pro CTG Leu ATG	GAT Asp 730 GAA Glu CAG Gln ACC Thr AGT Ser AAG Lys 810	Lys 715 CTT Leu  GAG Glu  AGA Arg  TTG Leu  TCA Ser 795 AGT Ser	23 23 24 24 25 25

216 217			Arg					Ile	GGT Gly				Gly				2667
218 219			830					835					840				
220									GTA						_		2715
221 222	Lys		Gln	Lys	Ile	Asn	G1n 850	Met	Val	Cys	Asn	Ser 855	Asp	Arg	vaı	Leu	
223		845					850					655					
224	AAA	AGA	AGT	GCT	GAA	GGA	AGC	AAC	CCT	CCT	AAA	CCA	CTG	AAA	AAA	CTA	2763
225	Lys	Arg	Ser	Ala	Glu	_	Ser	Asn	Pro	Pro		Pro	Leu	Lys	Lys		
226	860					865					870					875	
227 228	000	mmm	C A III	7 mm	(T 7 7	CCA	ma z	CAM	<i>C</i> 7 7	CCA	ריאיני	CCA	א כיידי	א א א	ር አጥ	CTC	2811
229									GAA Glu								2011
230	Arg	Pne	Asp	тте	880	GIA	261	Asp	GIU	885	Asp	GIY	261	цуъ	890	пец	
231					000					000							
232	CCA	GGA	GAG	TCC	AAA	TTT	CAG	CAG	AAA	CTG	GCA	GAA	ATG	ACT	TCT	ACT	2859
233	Pro	Gly	Glu	Ser	Lys	Phe	Gln	Gln	Lys	Leu	Ala	Glu	Met		Ser	Thr	
234				895					900					905			
235						~	~				~~~	200	3 m/3	a » m	3 CC	max.	2007
236									ATG								2907
237 238	Arg	Thr	910	мес	GIN	гув	GIII	ьуs 915	Met	ASII	Asp	Ser	920	Asp	1111	SET	
239			910					913					720				
240	AAC	AAG	GAA	GAG	AAA	TGAG	GAT	CTC A	AGGA	CCTT	G TO	GAC!	ACTG	r GTA	ACAC	CTCT	2962
241			Glu														
242		925															
243																	0004
244	GGAT	rtca:	rtg 1	rctc1	CAC	AG AI	rgtgi	ACTG	TAT				•				2994

- 1 36. A pharmaceutical composition of claim 32, wherein said RB cDNA fragment is selected from the group consisting of RB-1, RB-2, RB-5, y79R8 and mixtures
- 3 thereof.
- 1 37. A pharmaceutical composition of claim 32, wherein a resulting mRNA transcript of said RB cDNA fragment has 4.6 kb.
- 1 38. A pharmaceutical composition of claim 37, wherein the cloned genomic DNA has at least 27 exons.
- 39. A pharmaceutical composition of claim 30, wherein the cloned RB cDNA transcribes into mRNA which translates in protein having an amino acid sequence comprising:

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M P P K T P R K T A A T A A A A A A E P P A P P P P P P E E D P E
                                                     ( 34)
4
   QDSGPEDLPLVRLEFEETEEPDFTALCQKLKIPDHVRERA
                                                      (74)
5
   WLTWEKVSSVDGVLGGYIQKKKELWGICIFIAAVDLDEMS
                                                      (114)
6
   FTFTELOKNIEISVHKFFNLLKEIDTSTKVDNAMSRLLKK
                                                      (154)
7
                                                      (194)
   YDVLFALFSKLERTCELIYLTQPSSSISTEINSALVLKVS
                                                     (234)
   WITFLLAKGEVLQMEDDLVISFQLNLCVLDYFIKLSPPML
                                                     (274)
   LKEPYKTAVIPINGSPRTPRRGOMRSARIAKOLENDTRII
10
                                                     (314)
   EVLCKEHECNIDEVKNVYFKNFIPFMNSLGLVTSNGLPEV
11
                                                     (354)
   ENLSKRYEEIYLKNKDLDARLFLDHDKTLQTDSIDSFETQ
12
   RTPRKSNLDEEVNVIPPHTPVRTVMNTIQQLMMILNSASD
                                                     (394)
13
                                                     (434)
14
   OPSENLISYFNNCTVNPKESILKRVKDIGYIFKEKFAKAV
   GQGCVEIGSQRYKLGVRLYYRVMESMLKSEEERLSIQNFS
                                                     (474)
15
   KLLNDNIFHMSLLACALEVVMATYSRSTSQNLDSGTDLSF
                                                     (514)
16
                                                     (554)
   PWILNVLNLKAFDFYKVIESFIKAEGNLTREMIKHLERCE
17
   HRIMESLAWLSDSPLFDLIKQSKDREGPTDHLESACPLNL
                                                     (594)
18
                                                     (634)
   PLONNHTAADMYLSPVRSPKKKGSTTRVNSTANAETQATS
19
   AFOTOKPLKSTSLSLFYKKVYRLAYLRLNTLCERLLSEHP
                                                     (674)
20
   ELEHIIWTLFQHTLQNEYELMRDRHLDQIMMCSMYGICKV
                                                     (714)
21
                                                     (754)
   KNIDLKFKIIVTAYKDLPHAVQETFKRVLIKEEEYDSIIV
22
   FYNSVFMQRLKTNILQYASTRPPTLSPIPHIPRSPYKFPS
                                                     (794)
23
                                                     (834)
   SPLRIPGGNIYISPLKSPYKISEGLPTPTKMTPRSRILVS
24
                                                     (874)
   IGESFGTSEKFQKINQMVCNSDRVLKRSAEGSNPPKPLKK
25
                                                     (914)
26
   LRFDIEGSDEADGSKHLPGESKFQOKLAEMTSTRTRMQKQ
                                                     (928)
27
   KMNDSMDTSNKEEK
28
29
   single-letter abbreviations for the amino acid residues are:
30
   A, Ala; C, Cys; D, Asp; E, Gly; F, Phe; G, Gly; H, His;
31
   I, Ile; K, Lys; L, Leu; M, Met; N, Asn; P, Pro; Q, Gln;
32
   R, Arg; S, Ser; T, Thr; V, Val; W, Trp; and Y, Tyr.
33
                 A DNA nucleotide sequence comprising:
1
            40.
2
   TTCCGGTTTT TCTCAGGGGA CGTTGAAATT ATTTTTGTAA CGGGAGTCGG GAGAGGACGG
3
                                                         60
4
5
                                                        120
   GGCGTGCCCC GCGTGCGCGC GCGTCGTCCT CCCCGGCGCT CCTCCACAGC TCGCTGGCTC
6
7
   171
8
                  Met Pro Pro Lys Thr Pro Arg Lys Thr Ala Ala
9
                                              10
                    1
10
   219
11
   Thr Ala Ala Ala Ala Ala Glu Pro Pro Ala Pro Pro Pro Pro
12
13
                                           25
             15
                            20
14
   15
                                                        267
   Pro Pro Glu Glu Asp Pro Glu Gln Asp Ser Gly Pro Glu Asp Leu Pro
16
17
          30
                         35
18
19
   CTC GTC AGG CTT GAG TTT GAA GAA ACA GAA GAA CCT GAT TTT ACT GCA
                                                        315
20
   Leu Val Arg Leu Glu Phe Glu Glu Thr Glu Glu Pro Asp Phe Thr Ala
21
                                     55
                      50
       45
22
23
   TTA TGT CAG AAA TTA AAG ATA CCA GAT CAT GTC AGA GAG AGA GCT TGG
                                                        363
```

24 25 26	Leu 60	Cys	Gln	Lys	Leu	Lys 65	Ile	Pro	Asp	His	Val 70	Arg	Glu	Arg	Ala	Trp 75	
27 28 29 30														GGA Gly			411
31 '32 33 34														ATT Ile 105		GCA Ala	459
35 36 37 38														CAG Gln			507
39 40 41 42														GAA Glu			555
43 44 45 46														AAG Lys			603
47 48 49 50														TGT Cys			651
51 52 53 54														ATA Ile 185			699
55 56 57 58														GCT Ala			747
59 60 61														CAG Gln			795
62 63 64 65														ATG Met			843
66 67 68 69														TCA Ser		CGA Arg	891
70 71 72 73														AAA Lys 265		CTA Leu	939
74 75 76 77														CAT His			987
78 79 80 81														ATA Ile			1035
82 83 84														GAG Glu			1083

85 86 87 88															GAT Asp 330		1131
89 90 91 92 93															GAT Asp		1179
94 95 96 97															CTT Leu		1227
98 99 100 101															GTT Val		1275
102 103 104 105															GAT Asp		1323
106 107 108 109															AAT Asn 410		1371
110 111 112 113															TTT Phe		1419
114 115 116 117															GGA Gly		1467
118 119 120 121															GAA Glu		1515
122	ATO	G CT	r aa	A TC	A GA	A GA	A GA	A CGA	TTA	A TC	CAT	CAA	AA?	r TT	r AG	C AAA	1563
123 124 125	Met 460	Leu	Lys	Ser	Glu	Glu 465	Glu	Arg	Leu	Ser	11e 470	Gln	Asn	Phe	Ser	Lys 475	
126 127 128 129		-													GCT Ala 490		1611
130 131 132 133															CTT Leu		1659
134 135 136 137															AAT Asn		1707
138 139 140 141															GCA Ala		1755
142 143 144 145															GAA Glu		1803

146															TTT		1851
147 148	Arg	iie	met	GIU	560	ьeu	Ala	Trp	ьeu	565	Asp	ser	PIO	ьец	Phe 570	Asp	
149						ί											
150															CTT		1899
151	Leu	Ile	Lys		Ser	Lys	Asp	Arg		Gly	Pro	Thr	Asp		Leu	Glu	
152 153				575					580					585			
154	ጥርጥ	CCT	ጥርጥ	ССТ	СФТ	דע ע	СТТ	ССТ	מידים	CAG	ΔΔΤ	ДДТ	CAC	ACT	GCA	GCA	1947
155								•							Ala		131.
156			590					595					600				
157																	
158															TCA		1995
159	Asp		Tyr	Leu	Ser	Pro		Arg	Ser	Pro	Lys		Lys	Gly	Ser	Thr	
160		605					610					615					
161 162	7 00	COM	C C C N	አአጥ	m/cm	א כיתי	CCA	አአጥ	CCA	GNG	አ <i>ር</i> አ	ראא	CCN	ACC	TCA	GCC	2043
163															Ser		2043
164	620	9	, u	11011	501	625					630					635	
165																	
166	TTC	CAG	ACC	CAG	AAG	CCA	TTG	AAA	TCT	ACC	TCT	CTT	TCA	CTG	TTT	TAT	2091
167	Phe	Gln	Thr	Gln		Pro	Leu	Lys	Ser		Ser	Leu	Ser	Leu	Phe	Tyr	
168					640					645					650		
169		70 70 70	ama	m2 m	000	CITI N	aaa	m 2 m	ama	CCC	COLV	יזי א א	አ <b>ሮ</b> አ	CTT	TGT	CAA	2139
170 171															Cys		2133
172	цуъ	цуъ	vai	655	Arg	Deu	AIG	- y -	660	~-9	1100			665	O _I D	-	
173				000													
174	CGC	CTT	CTG	TCT	GAG	CAC	CCA	GAA	TTA	GAA	CAT	ATC	ATC	TGG	ACC	CTT	2187
175	Arg	Leu	Leu	Ser	Glu	His	Pro	Glu	Leu	Glu	His	Ile	Ile	Trp	Thr	Leu	
176			670					675					680				
177		<b>a</b>	a. a	7.00	C/D/C	<b>a</b>	70 77 CT	an a		~~~	CEC	7 m/3	707	CAC	N C C	CAT	2235
178 179															AGG Arg		2233
180	PILE	GIII				GIII	ADII.	GIU	туr	GIU	нец		Hr 9	ASP	44.9	1110	
			птъ	IIII								695					
181		685	nis	IIII	200		690					695					
181 182		685					690				r GG(		A TGO	CAA	A GTO	B AAG	2283
181 182 183	TTC	685 GAG	C CA	A ATT	r ATO	3 ATO	690 3 TGT	r TCC	CATO	TAT	Gly	C ATA			A GTO Val	Lys	2283
181 182 183 184	TTC	685 GAG	C CA	A ATT	r ATO	G ATO	690 3 TGT	r TCC	CATO	TAT		C ATA					2283
181 182 183 184 185	TTO Leu 700	685 GA( Asp	C CA/ Gln	A ATT	r Ard Met	G ATO Met 705	690 TG1 Cys	r TC( Ser	C ATO Met	3 TAT Tyr	Gly 710	C AT/	Cys	Lys	Val	Lys 715	
181 182 183 184 185 186	TTO Leu 700	685 GAG Asp	C CA/ Gln GAC	A ATT	r ATO Met AAA	ATO Met 705	690 G TGT Cys AAA	r TCC Ser ATC	C ATO Met ATT	TAT Tyr GTA	Gly 710 ACA	C ATA	Cys	Lys	Val GAT	Lys 715 CTT	2283 2331
181 182 183 184 185 186 187	TTO Leu 700	685 GAG Asp	C CA/ Gln GAC	A ATT	r ATO Met AAA Lys	ATO Met 705	690 G TGT Cys AAA	r TCC Ser ATC	C ATO Met ATT	TAT Tyr GTA Val	Gly 710 ACA	C ATA	Cys	Lys	Val	Lys 715 CTT	
181 182 183 184 185 186	TTO Leu 700	685 GAG Asp	C CA/ Gln GAC	A ATT	r ATO Met AAA	ATO Met 705	690 G TGT Cys AAA	r TCC Ser ATC	C ATO Met ATT	TAT Tyr GTA	Gly 710 ACA	C ATA	Cys	Lys	Val GAT Asp	Lys 715 CTT	
181 182 183 184 185 186 187 188 189 190	TTO Leu 700 AAT Asn	685 GAG Asp ATA Ile	G CA/ Gln GAC Asp	A ATT	Met  AAA  Lys  720	Met 705 TTC Phe	690 G TGT Cys AAA Lys	TCC Ser ATC Ile	E ATO Met ATT Ile	TYT GTA Val 725	Gly 710 ACA Thr	Ile Ile GCA Ala	Cys TAC Tyr	Lys AAG Lys	Val GAT Asp	Lys 715 CTT Leu	
181 182 183 184 185 186 187 188 189 190 191	TTC Leu 700 AAT Asn	685 GAG Asp ATA Ile	GAC Asp	A ATT	Met  AAA Lys 720  CAG	Met 705 TTC Phe	690 Cys AAA Lys	TTC  Ser  ATC  Ile	ATT Ile  AAA Lys	TAT Tyr GTA Val 725 CGT	Gly 710 ACA Thr	Ile GCA Ala	TAC Tyr	Lys AAG Lys AAA Lys	Val GAT Asp 730	Lys 715 CTT Leu GAG	2331
181 182 183 184 185 186 187 188 189 190 191	TTC Leu 700 AAT Asn	685 GAG Asp ATA Ile	GAC Asp	A ATT	Met  AAA Lys 720  CAG	Met 705 TTC Phe	690 Cys AAA Lys	TTC  Ser  ATC  Ile	ATT Ile	TAT Tyr GTA Val 725 CGT	Gly 710 ACA Thr	Ile GCA Ala	TAC Tyr	Lys AAG Lys AAA	GAT Asp 730	Lys 715 CTT Leu GAG	2331
181 182 183 184 185 186 187 188 189 190 191 192 193	TTO Leu 700 AAT Asn CCT Pro	685 GAC Asp ATA Ile CAT His	GAC Asp GCT Ala	A ATT	Met  AAA Lys 720 CAG Gln	Met 705 TTC Phe GAG Glu	690 Cys AAA Lys ACA Thr	TCC Ser ATC Ile TTC Phe	ATT Ile  AAA Lys 740	TYT  GTA  Val  725  CGT  Arg	Gly 710 ACA Thr GTT Val	Ile GCA Ala TTG Leu	TAC Tyr ATC Ile	Lys AAG Lys AAA Lys 745	GAT Asp 730 GAA Glu	Lys 715 CTT Leu GAG Glu	2331
181 182 183 184 185 186 187 188 189 190 191 192 193 194	TTO Leu 700 AAT Asn CCT Pro	685 GAC Asp ATA Ile CAT His	GAC Asp GCT Ala	CTT Leu GTT Val 735	Met  AAA Lys 720 CAG Gln	Met 705 TTC Phe GAG Glu	690 Cys AAA Lys ACA Thr	Ser ATC Ile TTC Phe	ATT Ile  AAA Lys 740  TAT	TYT  GTA  Val  725  CGT  Arg	Gly 710 ACA Thr GTT Val	GCA Ala TTG Leu	TAC Tyr ATC Ile	AAG Lys AAA Lys 745 ATG	GAT Asp 730 GAA Glu	Lys 715 CTT Leu GAG Glu	2331
181 182 183 184 185 186 187 188 189 190 191 192 193 194 195	TTO Leu 700 AAT Asn CCT Pro	685 GAC Asp ATA Ile CAT His	GAC Asp GCT Ala GAT Asp	CTT Leu GTT Val 735	Met  AAA Lys 720 CAG Gln	Met 705 TTC Phe GAG Glu	690 Cys AAA Lys ACA Thr	Ser ATC Ile TTC Phe	ATT Ile  AAA Lys 740  TAT	TYT  GTA  Val  725  CGT  Arg	Gly 710 ACA Thr GTT Val	GCA Ala TTG Leu	TAC Tyr ATC Ile	AAG Lys AAA Lys 745 ATG	GAT Asp 730 GAA Glu	Lys 715 CTT Leu GAG Glu	2331
181 182 183 184 185 186 187 188 189 190 191 192 193 194	TTO Leu 700 AAT Asn CCT Pro	685 GAC Asp ATA Ile CAT His	GAC Asp GCT Ala	CTT Leu GTT Val 735	Met  AAA Lys 720 CAG Gln	Met 705 TTC Phe GAG Glu	690 Cys AAA Lys ACA Thr	TTC Phe	ATT Ile  AAA Lys 740  TAT	TYT  GTA  Val  725  CGT  Arg	Gly 710 ACA Thr GTT Val	GCA Ala TTG Leu	TAC Tyr ATC Ile	AAG Lys AAA Lys 745 ATG	GAT Asp 730 GAA Glu	Lys 715 CTT Leu GAG Glu	2331
181 182 183 184 185 186 187 188 189 190 191 192 193 194 195 196 197 198	TTO Leu 700 AAT Asn CCT Pro	GAC Asp ATA Ile CAT His	GAC Asp GCT Ala GAT Asp 750	CTT Leu GTT Val 735 TCT Ser	Met  AAA Lys 720 CAG Gln ATT	Met 705 TTC Phe GAG Glu	690 Cys AAA Lys ACA Thr	TTC Phe	Met ATT Ile AAA Lys 740 TAT Tyr	TYT  GTA  Val  725  CGT  Arg  AAC  Asn	Gly 710 ACA Thr GTT Val TCG Ser	GCA Ala TTG Leu GTC	TAC Tyr ATC Ile TTC Phe 760	Lys  AAG Lys  AAA Lys  745  ATG Met	GAT Asp 730 GAA Glu	Lys 715 CTT Leu GAG Glu AGA Arg	2331
181 182 183 184 185 186 187 188 189 190 191 192 193 194 195 196 197 198 199	TTO Leu 700 AAT Asn CCT Pro GAG Glu CTG	685 GAC Asp ATA Ile CAT His TAT Tyr AAA Lys	GAC Asp GCT Ala GAT Asp 750 ACA	A ATT	Met  AAA Lys 720 CAG Gln ATT Ile	Met 705 TTC Phe GAG Glu ATA Ile	690 Cys AAA Lys ACA Thr GTA Val	TTC Phe 755	ATT Ile  AAA Lys 740 TAT Tyr	TYT  GTA  Val  725  CGT  Arg  AAC  Asn	Gly 710 ACA Thr GTT Val TCG Ser	GCA Ala TTG Leu GTC Val	TAC Tyr ATC Ile TTC Phe 760	Lys AAG Lys AAA Lys 745 ATG Met	GAT Asp 730 GAA Glu CAG Gln	Lys 715 CTT Leu GAG Glu AGA Arg	2331 2379 2427
181 182 183 184 185 186 187 188 189 190 191 192 193 194 195 196 197 198 199 200	TTO Leu 700 AAT Asn CCT Pro GAG Glu CTG	GAC Asp ATA Ile CAT His TAT Tyr	GAC Asp GCT Ala GAT Asp 750 ACA	A ATT	Met  AAA Lys 720 CAG Gln ATT Ile	Met 705 TTC Phe GAG Glu ATA Ile	690 Cys AAA Lys ACA Thr GTA Val	TTC Phe 755	ATT Ile  AAA Lys 740 TAT Tyr	TYT  GTA  Val  725  CGT  Arg  AAC  Asn	Gly 710 ACA Thr GTT Val TCG Ser	GCA Ala TTG Leu GTC Val	TAC Tyr ATC Ile TTC Phe 760	Lys AAG Lys AAA Lys 745 ATG Met	GAT Asp 730 GAA Glu CAG Gln	Lys 715 CTT Leu GAG Glu AGA Arg	2331 2379 2427
181 182 183 184 185 186 187 188 189 190 191 192 193 194 195 196 197 198 199 200 201	TTO Leu 700 AAT Asn CCT Pro GAG Glu CTG Leu	GAC Asp ATA Ile CAT His TAT Tyr AAA Lys 765	GAC Asp GCT Ala GAT Asp 750 ACA Thr	CTT Leu GTT Val 735 TCT Ser	Met  AAA Lys 720 CAG Gln ATT Ile	Met 705 TTC Phe GAG Glu ATA Ile	690 Cys AAA Lys ACA Thr GTA Val	TTC Phe TTC Phe 755	Met  ATT Ile  AAA Lys 740  TAT Tyr  GCT Ala	TYT  GTA  Val  725  CGT  Arg  AAC  Asn  TCC  Ser	Gly 710 ACA Thr GTT Val TCG Ser ACC Thr	GCA Ala TTG Leu GTC Val	TAC Tyr ATC Ile TTC Phe 760 CCC Pro	Lys  AAG Lys  AAA Lys  745  ATG Met  CCT Pro	GAT Asp 730 GAA Glu CAG Gln ACC Thr	Lys 715 CTT Leu GAG Glu AGA Arg TTG Leu	2331 2379 2427 2475
181 182 183 184 185 186 187 188 189 190 191 192 193 194 195 196 197 198 199 200 201 202	TTO Leu 700 AAT Asn CCT Pro GAG Glu CTG Leu TCA	GAC Asp ATA Ile CAT His TAT Tyr AAA Lys 765 CCA	GAC Asp GCT Ala GAT Asp 750 ACA Thr	CTT Leu  GTT Val 735  TCT Ser  AAT Asn	Met  AAA Lys 720 CAG Gln ATT Ile ATT Ile CAC	Met 705 TTC Phe GAG Glu ATA Ile TTG Leu	690 Cys  AAA Lys  ACA Thr  GTA Val  CAG Gln 770 CCT	TTC Phe 755	ATT Ile  AAA Lys 740  TAT Tyr  GCT Ala	TAT Tyr GTA Val 725 CGT Arg AAC Asn TCC Ser	Gly 710 ACA Thr GTT Val TCG Ser ACC Thr	GCA Ala TTG Leu GTC Val AGG Arg 775 AAG	TAC Tyr ATC Ile TTC Phe 760 CCC Pro	Lys AAG Lys AAA Lys 745 ATG Met CCT Pro	GAT Asp 730 GAA Glu CAG Gln ACC Thr	Lys 715 CTT Leu GAG Glu AGA Arg TTG Leu	2331 2379 2427
181 182 183 184 185 186 187 188 189 190 191 192 193 194 195 196 197 198 199 200 201 202 203	TTC Leu 700 AAT Asn CCT Pro GAG Glu CTG Leu TCA Ser	GAC Asp ATA Ile CAT His TAT Tyr AAA Lys 765 CCA	GAC Asp GCT Ala GAT Asp 750 ACA Thr	CTT Leu  GTT Val 735  TCT Ser  AAT Asn	Met  AAA Lys 720 CAG Gln ATT Ile ATT Ile CAC	Met 705 TTC Phe GAG Glu ATA Ile TTG Leu	690 Cys  AAA Lys  ACA Thr  GTA Val  CAG Gln 770 CCT	TTC Phe 755	ATT Ile  AAA Lys 740  TAT Tyr  GCT Ala	TAT Tyr GTA Val 725 CGT Arg AAC Asn TCC Ser	Gly 710 ACA Thr GTT Val TCG Ser ACC Thr	GCA Ala TTG Leu GTC Val AGG Arg 775 AAG	TAC Tyr ATC Ile TTC Phe 760 CCC Pro	Lys AAG Lys AAA Lys 745 ATG Met CCT Pro	GAT Asp 730 GAA Glu CAG Gln ACC Thr	Lys 715 CTT Leu GAG Glu AGA Arg TTG Leu	2331 2379 2427 2475
181 182 183 184 185 186 187 188 189 190 191 192 193 194 195 196 197 198 199 200 201 202	TTO Leu 700 AAT Asn CCT Pro GAG Glu CTG Leu TCA	GAC Asp ATA Ile CAT His TAT Tyr AAA Lys 765 CCA	GAC Asp GCT Ala GAT Asp 750 ACA Thr	CTT Leu  GTT Val 735  TCT Ser  AAT Asn	Met  AAA Lys 720 CAG Gln ATT Ile ATT Ile CAC	Met 705 TTC Phe GAG Glu ATA Ile TTG Leu	690 Cys  AAA Lys  ACA Thr  GTA Val  CAG Gln 770 CCT	TTC Phe 755	ATT Ile  AAA Lys 740  TAT Tyr  GCT Ala	TAT Tyr GTA Val 725 CGT Arg AAC Asn TCC Ser	Gly 710 ACA Thr GTT Val TCG Ser ACC Thr	GCA Ala TTG Leu GTC Val AGG Arg 775 AAG	TAC Tyr ATC Ile TTC Phe 760 CCC Pro	Lys AAG Lys AAA Lys 745 ATG Met CCT Pro	GAT Asp 730 GAA Glu CAG Gln ACC Thr	Lys 715 CTT Leu  GAG Glu  AGA Arg  TTG Leu  TCA Ser	2331 2379 2427 2475
181 182 183 184 185 186 187 188 189 190 191 192 193 194 195 196 197 198 199 200 201 202 203 204	TTC Leu 700 AAT Asn CCT Pro GAG Glu CTG Leu TCA Ser 780	GAC Asp ATA Ile CAT His TAT Tyr AAA Lys 765 CCA Pro	GAC Asp GCT Ala GAT Asp 750 ACA Thr	CTT Leu  GTT Val 735  TCT Ser  AAT Asn  CCT Pro	Met  AAA Lys 720 CAG Gln ATT Ile ATT Ile CAC His	Met 705 TTC Phe GAG Glu ATA Ile TTG Leu ATT Ile 785	690 Cys  AAA Lys  ACA Thr  GTA Val  CAG Gln 770 CCT Pro	TTC Phe TTC Phe TTC Phe TTC ATT TYT CGA ATG	Met  ATT Ile  AAA Lys 740  TAT TYT  GCT Ala  AGC Ser	TYT  GTA  Val  725  CGT  Arg  AAC  Asn  TCC  Ser  CCT  Pro	Gly 710 ACA Thr GTT Val TCG Ser ACC Thr TAC Tyr 790	GCA Ala TTG Leu GTC Val AGG Arg 775 AAG Lys	TAC Tyr ATC Ile TTC Phe 760 CCC Pro	AAG Lys AAA Lys 745 ATG Met CCT Pro	GAT Asp 730 GAA Glu CAG Gln ACC Thr	Lys 715 CTT Leu  GAG Glu  AGA Arg  TTG Leu  TCA Ser 795	2331 2379 2427 2475

207 208	Pro	Leu	Arg	Ile	Pro 800	Gly	Gly	Asn	Ile	Tyr 805	Ile	Ser	Pro	Leu	Lys 810	Ser		
209 210	CCA	יימיי	מממ	ΔͲͲ	тса	GAA	ССТ	СТС	CCA	ACA	CCA	ACA	AAA	ATG	ACT	CCA	26	519
211															Thr			
212	110	- y -	_	815		Olu	011	200	820				-1-	825				
213			•	<b>V Z Z</b>														
214	AGA	TCA	AGA	ATC	TTA	GTA	TCA	ATT	GGT	GAA	TCA	TTC	GGG	ACT	TCT	GAG	26	567
215															Ser			
216	5		830					835					840					
$\frac{1}{217}$																		
218	AAG	TTC	CAG	AAA	ATA	AAT	CAG	ATG	GTA	TGT	AAC	AGC	GAC	CGT	GTG	CTC	27	715
219															Val			
220	•	845		-			850			_		855						
221																		
222	AAA	AGA	AGT	GCT	GAA	GGA	AGC	AAC	CCT	CCT	AAA	CCA	CTG	AAA	AAA	CTA	27	763
223	Lys	Arg	Ser	Ala	Glu	Gly	Ser	Asn	Pro	Pro	Lys	Pro	Leu	Lys	Lys	Leu		
224	860					865					870					875		
225																		
226															CAT		28	311
227	Arg	Phe	Asp	Ile	Glu	Gly	Ser	Asp	Glu	Ala	Asp	Gly	Ser	Lys	His	Leu		
228					880					885					890		,	
229																		
230															TCT		28	359
231	Pro	Gly	Glu	Ser	Lys	Phe	Gln	Gln	Lys	Leu	Ala	Glu	Met		Ser	Thr		
232				895					900					905				
233																		
234															ACC		29	907
235	Arg	Thr	_	Met	Gln	Lys	Gln		Met	Asn	Asp	Ser		Asp	Thr	ser		
236			910					915					920					
237													· amar	. cm		amam	2.0	262
238						TGAC	GAT(	STC A	AGGAC	CTTC	iG TC	;GAC	ACTG:	r GTA	ACAC	rici	23	962
239	Asn	-	Glu	Glu	Lys													
240		925																
241	001-			naman	DON 01		ncimo:	, amar	ייו אל ח	•							2.0	994
242	GGATTCATTG TCTCTCACAG ATGTGACTGT AT												2.5	<i>,</i> , , ,				

- 1 41. A method of therapeutically treating inactive, mutative or absent 2 cancer suppressing genes comprising:
- treating said inactive, mutative or absent cancer suppressing genes with at least a portion of intact cancer suppressing genes.
- 1 42. A method of claim 41, wherein said cancer suppressing genes are each a substance selected from the groups consisting of RB genes, breast cancer suppressing
- 3 genes, Wilm's tumor suppressing genes, Beckwith-Wiedemann syndrome suppressing genes,
- 4 bladder transitional cell carcinoma suppressing genes, neuroblastoma suppressing genes,
- 5 small cell lung carcinoma suppressing genes, renal cell carcinoma suppressing genes,
- 6 acoustic neuroma suppressing genes, colorectal carcinoma suppressing genes, and mixtures
- 7 thereof.

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43. A method of claim 41, wherein said treating includes:

- treating said inactive, mutative or absent cancer suppressing gene with a substance selected from the group consisting of an RB gene, a portion of said gene, or a mixture thereof.
- 1 44. A method of claim 43, wherein said portion is selected from the group 2 consisting of RB cDNA, RB cDNA fragment, homologues thereof and mixtures thereof.
- 1 45. The method of claim 41, wherein the intact cancer suppressing gene, or portion thereof, is delivered to the site of a tumor by means of a retrovirus.
- 1 46. A method of claim 41, wherein the intact cancer suppressing gene, or a portion thereof, is delivered to the site of a tumor by a liposome.
- 1 47. A method of claim 41, wherein the location of said cancer suppressing gene is determined by utilizing a genetic marker.